WS13.1 Lung clearance index predicts time to pulmonary exacerbation in children with CF

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Lung Clearance Index (LCI) is a promising endpoint for use in CF clinical trials. Since correlation with validated clinical endpoints has not yet been established, we investigated the association between baseline LCI and risk of respiratory tract exacerbations (RTE) in children with CF.

Methods: During a prospective observational study, baseline LCI (N_2 washout), FEV_1 and CFQR respiratory domain ($CFQR_{res}$) were measured. RTE, defined as an increase in respiratory symptoms treated with IV antibiotics, were recorded during one year. Whether basline LCI predicted RTE was assessed with a Poisson regression model and Kaplan–Meier plots. LCI z-scores were calculated from values in 57 healthy children.

Results: In 63 children with CF (median age 12.4 years, range 5–19), mean LCI z-score was 5.3 (SD 4.6) and mean FEV_1 z-score –0.9 (SD 1.3). $CFQR_{res}$ correlated with LCI ($R = -0.43$, $p < 0.001$), but not with FEV_1 ($R = 0.24$, $p = 0.051$). In the 53 patients with a normal FEV_1, $CFQR_{res}$ and LCI were still correlated ($R = -0.44$, $p = 0.002$).

During the 12 months follow up, 25 patients (40%) experienced 47 RTE. LCI and FEV_1 were predictors of RTE. Time to first RTE decreased with worsening LCI quartiles (Log Rank test, $p < 0.001$). Similarly, compared to the quartile with the lowest LCI, yearly RTE rate ratio in increasing LCI quartiles was 2.8 (95%CI 0.6–13.9, $p = 0.205$), 4.7 (95%CI 1.0–21.4, $p = 0.046$) and 13.6 (95%CI 3.2–57.0, $p < 0.001$). In the group with normal FEV_1, LCI but not FEV_1 z-score was still a predictor of RTE.

Conclusion: Baseline LCI predicts the risk of RTE in children with CF, even in the subgroup with normal FEV_1. These data further support the use of LCI as surrogate outcome in CF clinical trials.

WS13.2 Lung clearance index (LCI) and airway infection in CF

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Introduction: Persistent colonisation with *Pseudomonas aeruginosa* (PA) and *Staphylococcus aureus* (SA) is associated with a decline in LCI in children.

Objective: To compare LCI in patients with; PA only Vs. PA plus another organism; and SA only Vs. SA plus another organism.

Methods: Stable CF patients from adult & paediatric Northern Ireland CF centres were recruited. LCI was derived from multiple breath washout, using 0.2%SF_6 and a modified Innocor™ device. All known pathogens present in sputum were recorded, as analysed by routine diagnostic culture. Mann-Whitney U tests were used.

Results: n = 84; mean (SD) age 23.0 (13.1) range 6–65 yrs; M: 49; 32% F508del homozygous (Table 1).

Table 1. Pathogens detected and LCI results

Pathogens detected	n (%)	Age (yrs), mean (SD)	LCI, mean (SD), range	FEV_1 % predicted, mean (SD)
PA only	24 (28.6)	27.8 (11.0)	11.5 (2.7) 6.6–16.8	67.8 (16.6)
PA plus other	11 (13.1)	20.0 (5.8)	10.2 (1.4) 8.0–12.6	78.5 (18.7)
SA only	14 (16.7)	17.9 (6.6)	8.5 (2.3) 5.4–13.6	78.5 (16.0)
SA plus other	9 (10.7)	22.0 (19.7)	8.9 (2.5) 6.2–13.1	81.3 (20.3)
No significant growth	26 (31.0)	22.9 (15.9)	7.3 (0.9) 5.8–8.9	86.0 (17.7)

LCI was highest (worst) in the PA only group. There was no significant difference in LCI between PA only and PA plus other groups; or between SA only and SA plus other groups. Compared to no significant growth, LCI was significantly higher in PA only ($p < 0.001$) and PA plus other ($p < 0.001$) groups. There was a trend towards a higher LCI in patients with SA only ($p = 0.055$) and SA plus other ($p = 0.06$).

Conclusions: In this study, another pathogenic organism in combination with PA or SA did not result in a significantly higher LCI. LCI detected differences and trends between those groups with infection and those with no significant growth.

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WS13.3 Lung clearance index: A tool to assess the response to intravenous treatment among children with cystic fibrosis

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Aim: To assess the relative sensitivity of FEV1 and LCI in the detection of improvement after IV treatment among CF children chronically colonized with pseudomonas aeruginosa; to compare the effectiveness of IV treatment, when it's administered on a regular basis, or for acute exacerbations.

Methods: Thirty-two children, chronically colonized with pseudomonas aeruginosa, were admitted to be given IV antibiotics for two weeks. Nineteen patients received a course of elective treatment (group A) and 13 patients received IV antibiotic regimens for an acute exacerbation (group B). Spirometry and multiple-breath-washout tests were performed before and one month after IV antibiotic treatment.

Results: Thirty-two CF patients (15 males) were requited. The mean age at admission was 9.90 years and the mean FEV_1 % predicted was 83.43.

FEV_1 did not change significantly after iv treatment ($p = 0.156$). LCI decreased by 15% ($p = 0.0001$). The mean LCI was changed significantly by 6% ($p = 0.018$) among patients of group A. On the contrary, spirometric parameters had no statistically significant changes in this group. Patients of group B showed significant improvement in most of the lung function parameters; mean LCI decreased by 26% ($p = 0.0001$). FEV_1% increased significantly by 10.36% ($p = 0.05$). The mean LCI difference was significantly greater in group B compared to group A ($p = 0.001$).

Conclusions: LCI is a more sensitive index than FEV_1 to assess the effectiveness of IV antibiotic treatment among children with CF. Administration of IV antibiotic regimens is more effective on ventilation distribution, when it is given for an exacerbation in comparison to administration on a regular basis.

WS13.4 Chest HRCT (cCT) score predicts later *Pseudomonas* infection in young children with cystic fibrosis

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The role of cCT scores in predicting a subsequent *Pseudomonas aeruginosa* (PsA) colonization has not been investigated.

Objective: To demonstrate that cCT Brody score in CF children PsA free predicts the risk of colonization in the following 6 years.

Methods: cCT scans performed in 80 pediatric CF patients between 2004 and 2007 in a single center were scored using the Brody II system. All patients were then closely monitored with at least 4 sputum culture/year for a period of 6 years. Chronic colonization by PsA was defined as 3 or more positive sputum cultures in one year. One-way ANOVA was used to determine mean's differences in cCT scores according to PsA status at baseline and after 6 years.

Results: Median age and mean FEV1% pred. at cCT were respectively 7.9 y and 83.3%. At baseline, 66.3% patients were PsA free, 23.7% had episodic PsA, 10% had chronic PsA. Six years later, 13 of patients PsA free or episodically infected at baseline became chronically colonized with PsA (group A) and 59 patients remained PsA free or exhibited episodic infections (group B).

Children in group A had a significantly worse CT score at baseline (Mean 19, SD 9.1) compared with patients in group B (Mean 10, SD 9.1), $F = 12.1$, $p < 0.001$. Significant differences between groups were found for bronchiectasis (Mean 20.6 vs 11.7; F 14.9, $p < 0.001$).

Conclusions: These results suggest that early lung structural damage precedes chronic PsA infection in young children with cystic fibrosis. cCT should be performed early to identify patients at higher risk of PsA colonization.